

Functional food for exercise performance: fact or foe?

Louise Deldicque and Marc Francaux

Université catholique de Louvain, Institut d'éducation physique et de réadaptation, Louvain-la-Neuve, Belgium

Correspondence to Marc Francaux, PhD, Place Pierre de Coubertin 1, 1348 Louvain-la-Neuve, Belgium
Tel: +32 10 47 44 57; fax: +32 10 47 20 93;
e-mail: marc.francaux@uclouvain.be

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Purpose of review

To present food components showing evidence for improved sport performance in the light of the scientific literature from the past 2 years.

Recent findings

Appropriate nutrition is essential for sport performance. Nutritional products containing carbohydrates, proteins, vitamins, and minerals have been widely used by athletes to provide something extra to the daily allowance. Currently, the field of interest is shifting from macronutrients and fluids to physiologically active isolated food components. Several of them have been demonstrated to improve sport performance at a higher level than expected with a well balanced diet. In the present review, we will focus on the benefits of creatine, caffeine, branched-chain amino acids, and more particularly leucine, beta-alanine, bicarbonate, and glycerol ingestion on exercise performance.

Summary

A bulk of products is sold on the market labeled with various performance benefit statements without any scientific evidence. These food components are often used without a full understanding or evaluation of the potential benefits and risks associated with their use. There is thus a real need to classify food components on the basis of their evidence-based effectiveness.

Keywords

beta-alanine, bicarbonate, branched-chain amino acids, caffeine, creatine

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Introduction

Functional foods are foods or dietary components that may provide a health benefit beyond basic nutrition. It is already known that the appropriate selection of carbohydrates, proteins, and fluids as well as their timing of intake may favorably influence sport performance [1–6]. More recently, the field of interest has shifted from macronutrients and fluids to isolated food components. The purpose of this review is to present food components showing evidence for an improved performance in humans with a special focus on the literature of the past 2 years (Table 1). Although some others could potentially be helpful for health and recovery, such as vitamins, antioxidants, glucosamine/chondroitin, omega-3, ribose, pyruvate, and carnitine, we will not develop them further as there is not sufficient scientific evidence for improving sport performance thus far, if energy intake is high enough and if a varied diet is consumed.

Creatine

Creatine is a nonessential dietary element found in high abundance in meat and fish. Normal daily intake of creatine from an omnivorous diet approximates 1 g. Creatine is also synthesized within the body, primarily

in the liver, at a rate of about 1 g per day [7]. Synthetic supplements exist as creatine monohydrate or various creatine salts, such as creatine citrate or creatine pyruvate, the latter being more soluble than creatine monohydrate. Muscle creatine content averages 110–120 mmol/kg dry mass and can be increased up to 130–160 mmol/kg dry mass after creatine supplementation, which represents an increase of about 15–30% [7–13]. The first study to investigate the cell signaling induced by creatine in humans was published elsewhere [11]. Two strategies of supplementation exist. In most conditions, 20 g creatine are ingested every day for 5 days; thereafter, 3–5 g are consumed daily to maintain its muscle uptake [14]. A second strategy omits the loading phase. In this case, the rise in muscle creatine content is slower, but reaches the same level after about 15 days [14].

Creatine appears to be the most effective nutritional supplement currently available in terms of improving lean body mass [15–19] and anaerobic capacity [20–22]. To date, several hundred studies have been conducted to evaluate the efficacy of creatine supplementation in improving exercise performance [22]. Nearly 70% of these studies have reported a significant improvement in exercise capacity. The average gain in

Table 1 Food components showing scientific evidence for an improved performance

	Ergogenic effect	Recommended dose
Creatine	Stimulates muscle strength and power Increases lean body mass <i>Accelerates recovery after endurance exercise</i>	20–30 g for 5–7 days or 2–3 g for 1 month
Caffeine	Enhances endurance performance Improves strength performance Improves reaction time, alertness, and visual information processing	3–6 mg/kg 1 h before exercise 1–2 mg/kg
Branched-chain amino acids Leucine	Improve muscle protein balance Diminish muscle soreness after exercise Enhance endurance performance <i>Improve muscle strength</i>	0.3–0.5 g/kg before or immediately after exercise
Beta-alanine Bicarbonate Glycerol	Improves high-intensity performance Improves high-intensity performance Favors hyperhydration and rehydration <i>Increases endurance performance in warm environment</i>	4.8–6.4 g for 2–10 weeks 300 mg/kg 1 h before exercise 2–3 g/kg for 5–7 days

Ergogenic effects in *italic* are likely but need further research to be corroborated.

performance from these studies typically ranges between 10 and 15% depending on the variable of interest. A recent study [23] has evaluated the potential differential effect of oral creatine pyruvate and creatine citrate supplementation on exercise performance in healthy young athletes. Performance during intermittent hand-grip exercise of maximal intensity was evaluated before and after 4 weeks of 5 g creatine per day under each form. Participants performed 10 15 s exercise intervals, each followed by 45 s rest periods. Both creatine pyruvate and citrate increased mean power over all intervals suggesting that the form of creatine ingested is not essential for power improvement. Other recently published studies [24,25] tested the effect of creatine monohydrate on muscle strength, lean body mass, fiber area, and contractile protein content after 10-week resistance training. Whatever the form of creatine ingested, it has become evident that it has some positive effect on muscle strength and lean body mass. However, the effectiveness seems to dim after several months probably due to a downregulation of creatine transporters [26].

Creatine has a direct effect on performance but it can also indirectly improve performance by reducing muscle damage and inflammation and accelerating recovery after the exercise sessions. Twenty grams of creatine for 5 days prior to a half-ironman competition limited the increase in the proinflammatory cytokines IL-1 β , TNF α and IFN α as well as the prostaglandin E2 at 24 and 48 h after competition [27 \bullet]. However, oral creatine supplementation did not reduce skeletal muscle damage or enhance recovery following a hypoxic resistance exercise challenge [28]. As supplementation protocols were similar between both studies, one could postulate that creatine favors recovery from strenuous endurance exercise but not from resistance exercise.

Most studies have focused on the ergogenic effects of creatine supplementation in combination with resistance

exercise. Only a few studies have tried to determine the mode of action of creatine for increasing muscle mass. Although some molecular targets are affected by creatine supplementation itself [8,11,12,29,30], it appears that the most obvious effects are observed after several weeks of supplementation in combination with a resistance exercise programme. A recent study [31] reported that 4–16 weeks of creatine supplementation potentiates the increase in satellite cell number and their activation induced by exercise training. This is the first study to show a greater activation of satellite cells by creatine after several weeks of strength training in human. It remains to determine the mechanisms of activation of the satellite cells by creatine, which is a promising research area for future studies. Several clues have already been found in our laboratory using an in-vitro model [32 \bullet ,33].

Caffeine

Caffeine is the most commonly consumed drug in the world and the health risks are minimal. The main sources of caffeine are coffee, tea, mate, guarana, and soft drinks. It appears that ingesting a dose of 3–6 mg/kg 1 h before exercise is optimal, as plasma concentrations approximate a maximum level in 1 h [34] and the ergogenic effect is maintained for at least 3 h [35]. It is of note that two metabolized products of caffeine, paraxanthine and theophylline, are other potent performance enhancing components [36,37].

The dominant dogma accounting for the ergogenic properties of caffeine has involved muscle glycogen sparing by increasing fat metabolism [38]. Many studies have thus been conducted to test the beneficial effect of caffeine in activities in which glycogen is a limiting factor. The ergogenic effect of caffeine in endurance performance is now well established for activities lasting from 60 s to 2 h [39–42], whereas it is only being studied in strength activities following promising prior reports showing

enhanced myoneural function and contractility [43–48]. A few recent studies have been conducted to test the efficacy of caffeine on one repetition maximum (1-RM) performance. Compared with placebo, greater 1-RM bench press was demonstrated in resistance-trained men after ingestion of a caffeine-containing supplement, yet no difference in leg press 1-RM was found [49]. Jacobs *et al.* [50] revealed no effect of caffeine ingestion (4 mg/kg) on repeated bench or leg-press exercises to exhaustion. A very recent study [51] showed that there was no effect of caffeine (6 mg/kg) on 1-RM bench and leg press nor was an effect of caffeine on total weight lifted during a 60% 1-RM trial. Further studies are thus required to clarify if caffeine is able to enhance 1-RM.

In addition to its effect on endurance, low doses of caffeine (1–2 mg/kg) can also have benefits on reaction time, alertness, and visual information processing [52]. The physiological mechanisms of action of caffeine are only poorly understood. The most physiological effect of caffeine is mediated by the inhibition of adenosine receptors [53], which are found in most tissues, and by the stimulation of adrenaline secretion [54]. As mentioned above, caffeine has been shown to stimulate fat oxidation leading to a reduction in the rate of muscle glycogen utilization, but this does not appear to explain changes in performance. Caffeine likely exerts its beneficial effect on performance by reducing perception of fatigue and improving muscle fiber recruitment [39,40]. This issue has been tested by two recent studies [55,56], in which participants were asked to cycle for approximately 2 h at 60–75% $\text{VO}_{2\text{max}}$ in a warm environment. In the study of Cureton *et al.* [55], participants received caffeine (5.3 mg/kg) under the form of a sport drink during the 2 h trial, whereas in the study of Del Coso *et al.* [56], participants received a pill containing 6 mg/kg. Before and after exercise, maximal voluntary contraction, voluntary activation, and electrically evoked contractile properties of the quadriceps were determined. In both studies, caffeine prevented a significant decrease in quadriceps maximal voluntary contraction at the end of the trial. However, an increase in voluntary activation, reflecting an improvement of the central nervous system (CNS), without any change in electrically evoked contractile properties was only observed in the study of Del Coso *et al.* [56]. The latter result enforces the hypothesis that caffeine's effects are directed to the CNS. On the contrary, the results of Cureton *et al.* [55] suggest a direct effect of caffeine on the muscle as evoked torque was increased and voluntary activation was unaffected. The contrasting results between both studies can be partially explained by methodological concerns such as the form of caffeine ingested, (included in a sports drink containing other active compounds or not) and the timing of caffeine ingestion (small doses throughout the exercise or one

bolus 45 min before). The mechanisms of the ergogenic effects of caffeine are still under debate.

Branched-chain amino acids, leucine and beta-hydroxy-beta-methylbutyrate

The branched-chain amino acids (BCAAs) leucine, isoleucine, and valine make up more than one-third of muscle protein [57]. Dairy and red meat are good sources of BCAA, as well as whey, protein and eggs. BCAAs are extensively used among bodybuilders and strength athletes to promote muscle hypertrophy and strength, and to diminish muscle soreness that usually follows exercise [58]. As BCAAs, and particularly leucine, undergo increased oxidation during prolonged endurance exercise, BCAAs supplementation has also been found to be beneficial during and after such type of exercise, possibly by limiting the increase in the ratio-free tryptophan/BCAAs, thereby reducing central fatigue [59,60].

The mechanism of action of BCAA on muscle hypertrophy has been shown to occur by both a reduction in protein breakdown and a stimulation of protein synthesis in rats [61] but it is far to be confirmed in humans. The improvement in protein balance following BCAAs administration in humans seems to occur only via a decreased protein degradation [62,63]. It is possible that to promote protein synthesis in human skeletal muscle, BCAAs must be coupled to resistance exercise as, in this case, signaling events leading to protein synthesis are activated [64]. Following observations in rats [65–70], it has been suggested that the effect of BCAAs could be attributable to leucine alone. One recent human study [71] has compared the effectiveness of a drink containing carbohydrates (0.3 g/kg per h), or carbohydrates (0.3 g/kg per h) and a protein hydrolysate (0.2 g/kg per h), or the same amount of carbohydrates and proteins and free leucine (0.1 g/kg per h) in stimulating net protein accretion after resistance exercise. The third beverage, containing leucine, was the most effective in improving net protein balance as well as in increasing plasma insulin concentration and muscle fractional synthetic rate. Leucine could indirectly stimulate protein synthesis via an increase in plasma insulin but it could also function as a nutritional signaling molecule that modulates muscle protein synthesis, breakdown or both following food intake. In rats, the stimulatory effect of leucine on protein synthesis occurs at the level of translation initiation and involves signaling through mammalian target of rapamycin (mTOR) [72]. mTOR is thought to serve as a convergence point for leucine-mediated and insulin-mediated effects on translation initiation [73,74]. Two very recent studies [75,76] showed that mTOR signaling and protein synthesis were increased by a leucine-enriched beverage containing amino acids and carbohydrates. Unfortunately, the authors compared the group

receiving this drink with a group receiving no nutrients. Thus, the protocol did not allow estimating the likely additional effects of leucine to those of proteins and carbohydrates. The way by which human muscle cells sense an increase in leucine to activate mTOR signaling is currently unknown but recent studies suggest that the kinases hVps34 and mitogen-activated protein kinase kinase kinase-3 (MAP4K3) may be involved [77,78,79^{••},80,81].

The effect of leucine on protein metabolism could be mediated by one of its metabolites, namely beta-hydroxy-beta-methylbutyrate (HMB). A number of studies have indicated that HMB supplementation may elicit several ergogenic benefits, including anticatabolic [82], anabolic [83], and lipolytic effects [84]. Thus, it has been suggested that HMB may partly be responsible for the benefits of leucine supplementation [85].

Beta-alanine

Beta-alanine, a nonproteogenic amino acid essentially found in meat and fish, is the limiting substrate to carnosine synthesis. Carnosine is a dipeptide (beta-alanyl-L-histidine) found in high concentrations in skeletal muscle (10–20 mmol/kg dry mass) [86] where it acts as a pH buffer [87]. Carnosine content is up to two times higher in fast-twitch (type II) compared with slow-twitch (type I) muscle fibers [88] and may be increased by 40–80% by 2–10 weeks ingestion of 4.8–6.4 g beta-alanine per day [89,90,91[•]] or by prolonged intense physical training [92,93]. It is of note that basal carnosine concentrations are higher in sprinters than in marathon runners or untrained people [94].

Beta-alanine supplementation is taken by athletes to increase skeletal muscle carnosine levels, which potentially could augment buffering capacity, delay fatigue, and improve exercise performance. Indeed, several studies performed in laboratory and developed to decrease muscle pH showed that increasing muscle carnosine content can aid performance. Suzuki *et al.* [95] observed a significant relationship between the carnosine concentration in human skeletal muscle and 30 s high-intensity exercise performance. More recently, 10-week beta-alanine supplementation has been shown to result in an increased time to exhaustion in a cycling test performed at 110% of power output at maximal heart rate (HR) [90]. In another study [96], beta-alanine supplementation improved time to exhaustion during isometric exercise at 45% of maximal voluntary contraction, which corresponds to the work level resulting in the largest increase in lactate and pyruvate contents in muscle [97] and likely to the largest decline in intramuscular pH. Beta-alanine supplementation has also been tested for improving endurance performance [98]. Although maximal oxygen consumption was not changed

after 4-week supplementation, time to exhaustion during maximal cycle ergometry performance was increased and the onset of neuromuscular fatigue and that of the ventilatory threshold at submaximal workloads were delayed, conceivably as a result of an increased buffering capacity [98].

In contrast to the studies performed in laboratories, only limited work has been carried out in the field. Although 4-week beta-alanine supplementation attenuated fatigue in repeated bouts of exhaustive dynamic contractions in trained sprinters, it did not improve 400 m running performance [91[•]]. Kendrick *et al.* [99] analyzed the effect of 10 weeks of resistance training combined with beta-alanine supplementation on whole-body strength, force production, muscular endurance and body composition. Increasing muscle carnosine content did not result in an improved training effect on force production and muscle hypertrophy through whole-body resistance training. The authors argued that it is possible that the time under tension was not long enough to produce a significant accumulation of proton or that the training effect on performance was more than that resulting from changes in buffering and therefore masked any ergogenic effect from beta-alanine supplementation. In summary, the benefits of beta-alanine supplementation only hold true at exercise intensities in which a decrease in muscle pH is exerting a limiting effect on exercise performance.

Bicarbonate

As mentioned above, carnosine is an important buffer in the muscle. During intense exercise, the intracellular buffers are insufficient to buffer all the hydrogen ions formed, which are released into the circulation. Extracellular bicarbonate helps buffer these ions and increases the gradient for efflux of hydrogen ions from the cells. Increasing the body's buffer capacity by increasing the extracellular bicarbonate concentration reduces acidosis and thereby delays fatigue [100,101]. Moreover, ingestion of 300 mg/kg [102] sodium bicarbonate improves high-intensity performance in most studies [103], more particularly short-duration (5–15 s) repeated sprint performance [104–106]. Because sodium bicarbonate may cause gastrointestinal discomfort in some athletes, sodium citrate and sodium lactate, which can produce an indirect buffering effect by consuming protons when metabolized, have also been tested. It seems that ingestion of sodium bicarbonate is the most effective in increasing sprint performance [107]. Recently, sodium bicarbonate has also been shown to improve swimming [108] and judo [109] performance.

Glycerol

Glycerol is an osmotically active molecule that is used to optimize hydration status for the purpose of improving

performance in warm conditions. It is a well tolerated agent that does not approach toxic levels when administered orally in doses of below 5 g/kg [110]; however, glycerol may cause gastrointestinal discomfort, headache, and blurred vision when used for hyperhydration before exercise [111–113]. A recent meta-analysis [114] determined that glycerol-induced hyperhydration clearly enhanced fluid retention better than water-induced hyperhydration. This ergogenic effect of glycerol on hydration has been shown to increase performance or time to exhaustion in both temperate or warm environments [113,115–117], to increase sweat rate [118] and to decrease HR [117] and rectal temperature during moderate-intensity cycling exercise [115]. The beneficial effect of glycerol on hydration status can last for up to 32–48 h after dosing [119]. Easton *et al.* [120^{*}] tested the combined effect of creatine (2×11.4 g/day) and glycerol (2×1 g/kg per day) supplementation for 7 days before one exercise trial in the heat. The addition of glycerol to creatine increased total-body water more than creatine or glycerol alone but it did not further enhance the attenuation in HR rectal temperature during exercise compared with glycerol alone. Hyperhydrating before exercise through creatine, glycerol or both did not result in any significant improvement in 16.1 km time trial performance compared with euhydration. Several other previous studies [121–124] did not observe any improvement in performance following glycerol-induced hyperhydration, other studies [111–113,116,117,121] did not find any thermoregulatory benefit.

Although there is a vast amount of information on the role of glycerol as a hyperhydration agent, very limited data are available on its effect in rehydration [125]. Recently published data showed that rehydration with glycerol increased time to exhaustion during intensive cycling in the heat, likely by maintaining greater plasma volume. However, glycerol did not provide any cardiovascular or thermoregulatory advantages [126]. In summary, glycerol supplementation can be an effective ergogenic aid in case of potential high dehydration (>3–4% body mass) caused by hot and wet environmental conditions and long duration exercise but not in case of euhydration or modest dehydration.

Conclusion

Many food products are sold in the market but only a few display sufficient scientific backgrounds to be used properly and efficiently for improving performance (Table 1). Amongst the well documented food components, creatine is one of the most popular and is used to increase muscle strength and power as well as lean body mass. Caffeine enhances endurance performance and improves reaction time, alertness, and visual information processing. BCAAs, and more particularly leucine, improve

muscle protein balance. Buffering or precursors of buffering agents, such as bicarbonate and beta-alanine, are useful to increase high-intensity performance. Finally, glycerol can favor hyperhydration and rehydration in warm environments. Although these food components have proven their efficacy, it should be kept in mind that they only partially contribute to performance and do not compensate for an absence of talent or a lack of training or motivation. The place of nutrition is small but is essential to help the talented and motivated individuals to make the most of their potential.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 815).

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